The Coexistence of Generalized and Lateralized Periodic Discharges: Report of Two Adult Cases with SSPE and MELAS Syndrome

Jeneralize ve Lateralize Periyodik Deşarjların Birlikteliği: SSPE ve MELAS Sendromlu İki Erişkin Olgu Sunumu

Aslıhan Taşkıran, Serap Saygı

Hacettepe Üniversitesi Tıp Fakültesi, Nöroloji Anabilim Dalı, Ankara, Türkiye

Turk Norol Derg 2011;17:161-166

ÖZET

Bugüne kadar jeneralize ve lateralize periyodik deşarjların aynı EEG trasesinde eş zamanlı olarak ortaya çıkışı bildirilmemiştir. Burada, subakut sklerozan panensefalit ve MELAS sendromu gibi oldukça ender karşılaşılan tanılar almış iki erişkin olgu sunulacaktır. Her iki hastanın EEG'sinde eş zamanlı jeneralize ve lateralize periyodik deşarjlara rastlanmıştır. EEG görünümü benzer olmasına rağmen, intravenöz diazepam enjeksiyonu sonrası subakut sklerozan panensefalit olgusunda deşarjlar daha belirgin hale gelmiş, MELAS sendromlu olguda ise baskılanmıştır. Her iki hastada posterior yerleşimli lezyonları gösteren beyin MRG incelemesinde, subakut sklerozan panensefalit olgusunda subkortikal beyaz cevherin, MELAS sendromlu olguda ise korteksin ön planda tutulduğu görülmüştür. Ayrıca, MELAS sendromunda jeneralize periyodik deşarjlar ilk kez bildirilmektedir. Periyodik deşarjları oluşturan mekanizmalar henüz tam olarak anlaşılamamıştır. Sunulan olguların, bu ender rastlanan EEG görünümlerini anlamaya katkı sağlayacağı düşünülmektedir.

Anahtar Kelimeler: Elektroensefalografi, subakut sklerozan panensefalit, MELAS sendromu.

ABSTRACT

The Coexistence of Generalized and Lateralized Periodic Discharges: Report of Two Adult Cases with SSPE and MELAS Syndrome

Aslıhan Taşkıran, Serap Saygı

Department of Neurology, Faculty of Medicine, University of Hacettepe, Ankara, Turkey

Generalized and lateralized periodic discharges have not been reported previously in the same EEG simultaneously. Here, we report two adult patients who suffered from rare clinical conditions [subacute sclerosing panencephalitis (SSPE) and nitochondrial myopathy, encephalopathy, lactic acidosis, and stroke-like episodes (MELAS) syndrome]. Their EEGs showed the same pattern consisting of ge-

neralized periodic discharges and lateralized periodic discharges in the same EEG simultaneously. Although the appearances of the EEG were very similar, discharges became more prominent after intravenous diazepam injection in the case with SSPE but were suppressed in the case with MELAS. Lesions in the magnetic resonance imaging (MRI) were located posteriorly in both patients, involving mainly subcortical white matter in the case with SSPE, but mainly the cortical area in the case with MELAS. Generalized periodic discharges are also reported in MELAS for the first time. The underlying mechanisms of the genesis of periodic discharges are still not known, and these two patients may help us to learn more about these rare patterns.

Key Words: Electroencephalography, subacute sclerosing panencephalitis, MELAS syndrome.

INTRODUCTION

Periodic electroencephalographic patterns are classified as generalized or lateralized according to their topographic distribution (1). Generalized periodic epileptiform discharges (GPEDs) are rare findings seen in a variety of pathological states and can be classified as long- interval (longer than 4 seconds) or short-interval (shorter than 4 seconds) GPEDs according to the interval of the periodic discharges (1,2). According to the nomenclature proposed by the American Clinical Neurophysiology Society subcommittee recently, GPEDs are now termed as generalized periodic discharges (GPDs) (3). For the purpose of standardization, the new terminology will also be used in this paper.

Subacute sclerosing panencephalitis (SSPE) is one of these occasions in which the periodic complexes tend to appear with long intervals (4-30 seconds) and shorten as the disease progresses (1,4). Although some degree of asymmetry and focal abnormalities can be seen in some SSPE patients, the periodic complexes are symmetrical and synchronous in the majority of the cases (1,4,5).

Mitochondrial encephalopathies are another group of medical conditions associated with abnormal EEG findings. The most common feature was reported to be the slowing of the alpha rhythm in one study (6). In the patients with MELAS syndrome (mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke-like episodes), regional epileptiform discharges are recorded over the affected brain area (7). In terms of periodic discharges, periodic lateralized epileptiform discharges (PLEDs) are known patterns of MELAS and associated with partial seizures, including epilepsia partialis continua and complex partial status epilepticus (8-11). Here again, the new term lateralized periodic discharges (LPDs) is used herein instead of "PLEDs", in accordance with the American Clinical Neurophysiology Society.

The presence of lateralized and generalized periodic discharges in the same record simultaneously has not been reported previously. Here, we present two different cases, one with the diagnosis of MELAS syndrome and the other with the diagnosis of SSPE, having GPDs and LPDs concurrently in the same EEG traces.

CASES

Case 1

A 24-year-old woman admitted with a two-year history of myoclonic jerks associated with drop attacks and progressive cognitive decline. She had experienced seizures with vocalization and loss of consciousness for two years. Personal and family history were unremarkable. Her neurologic examination revealed ataxia, dysarthria and mild spastic quadriparesis. Myoclonic jerks were observed during the examination. The EEG obtained in her full conscious state showed periodic generalized slow and slow sharp waves with 5-7-second intervals, which became prominent after diazepam injection, and another ongoing periodic activity, LPDs on the right occipital area (Figure 1a, 1b). The magnetic resonance imaging (MRI) revealed hyperintense lesions in bilateral posterior areas, but with prominence on the right occipital lobe, mostly involving white matter (Figure 2). Measles IgG level was elevated (3.5 RU/mL) in the cerebrospinal fluid (CSF). After this investigatory work-up, she was diagnosed as SSPE.

Case 2

A 33-year-old man admitted to our hospital with problems in speech and vision. He had had difficulty in finding words for two months. In a few days, total visual loss developed. He was diagnosed to have cerebrovascular disease in another hospital and antiaggregant therapy was started. A right-sided hemiparesis and bilateral hearing loss had developed, and he had become totally unable to walk and had been aphasic (receptive type) in one week. On neurologic examination, he was found to have impaired comprehension, bilateral cortical blindness and severe bilateral hearing loss. Bilateral Babinski signs were present without obvious lateralized motor deficit. He was ataxic. In the EEG obtained in his full conscious state, there was a periodic activity of generalized slow and slow sharp waves with 8-10-second intervals, and LPDs consisting of sharp waves at a 0.7-1 Hz frequency on the right occipital electrodes (Figure 3a). After intravenous (IV) diazepam injection, periodic epileptiform discharges disappeared for a few minutes (Figure 3b). MRI of the patient revealed right parietooccipital cortical acute infarction, right temporal and lateral parietal, and left temporopari-

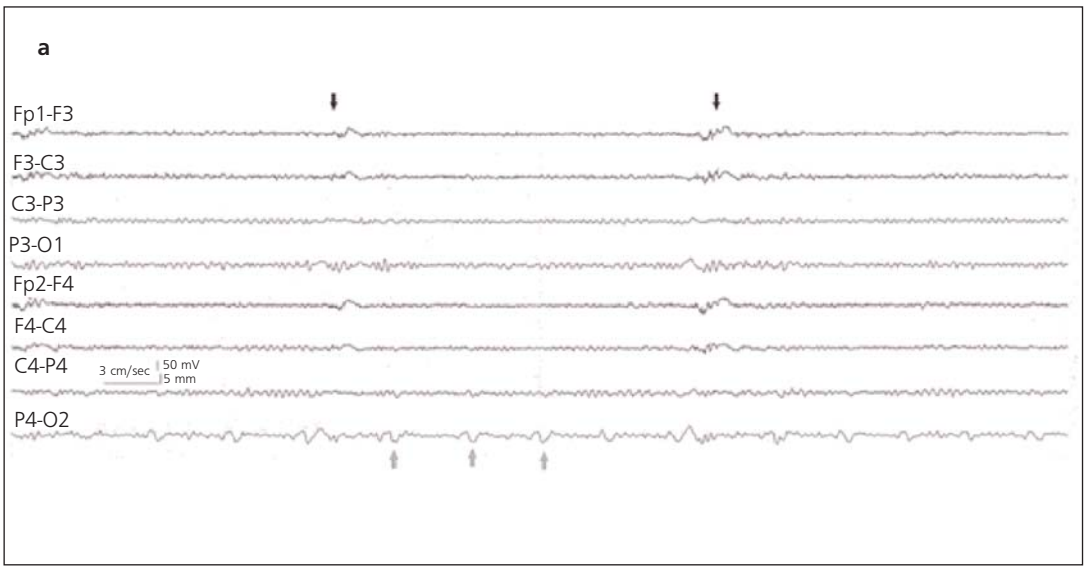

Figure 1a. EEG of the patient with SSPE: a) The EEG showed GPDs consisting of slow and slow sharp waves with 5-7-second intervals associated with myoclonic jerks and right LPDs.

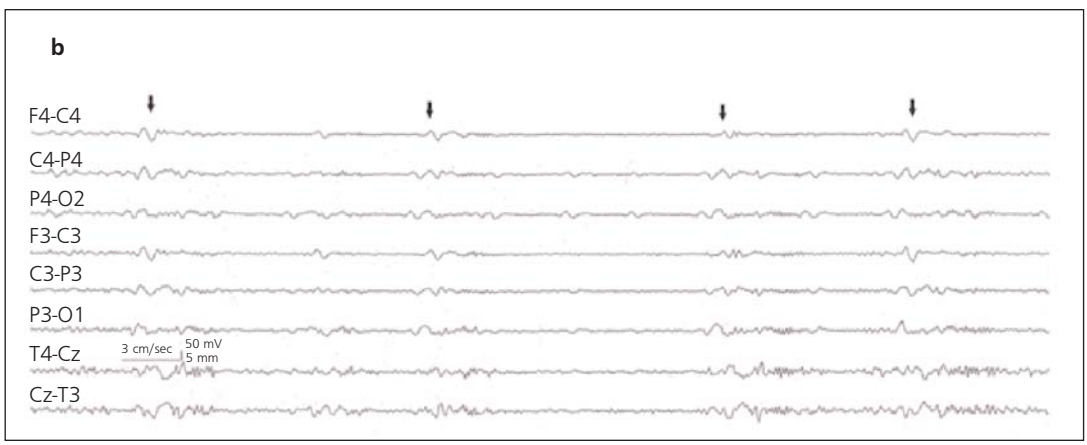

Figure 1b. After IV diazepam injection, GPDs became more prominent and the interval was shortened. Black and grey arrows indicate GPDs and LPDs, respectively. HF: 35 Hz; LF: 0.5 Hz (GPDs, generalized periodic discharges; LPDs, lateralized periodic discharges; SSPE, subacute sclerosing panencephalitis).

etooccipital subacute infarctions, mostly involving cortical regions with cerebral and cerebellar atrophies (Figure 4). CSF findings included high lactate level (46.1 mmol/L) and a high lactate/pyruvate ratio (46.1/1.6) as in the serum of the patient (lactate = 35 mmol/L, pyruvate = 1.1 mg/dL). Muscle biopsy was performed and revealed severely degenerated muscle cells and ragged red fibers. The patient was diagnosed as MELAS, which was further confirmed with genetic analysis of the 3243 MELAS mutation.

DISCUSSION

These two patients showed the same electrophysiological features on EEGs with totally distinct diagnoses, response to benzodiazepines and common property raises the question of whether there is another common feature underlying these electrophysiological findings. It is clear that the pathophysiology of SSPE and MELAS involve different processes; however, when localization of the lesions is considered, there may be a relation.

It was postulated that periodic discharges were a consequence of extensive white matter damage disconnecting the cortex from its normal afferent input (4). Most of the explanations attributed a major role to white matter in the genesis of periodic discharges seen in the cases with SSPE (1). On the other hand, Gloor et al. reported patients exhibiting periodic discharges without post-mortem evidence of exclusive white matter disease, but with diffuse grey matter disease (12). They assumed that the central nervous system was in an abnormal functional sta-

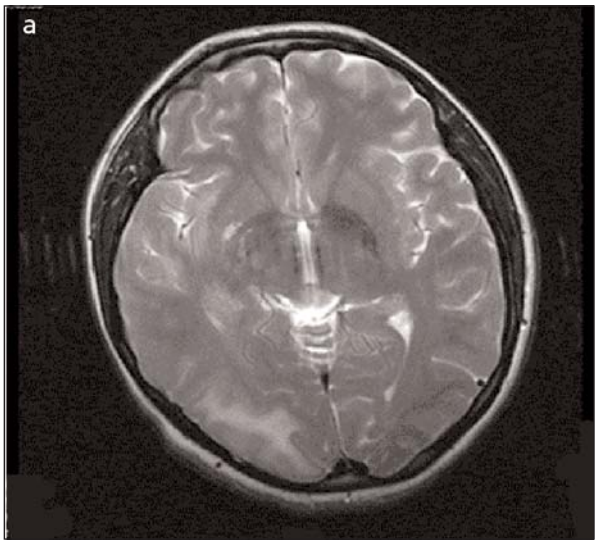

Figure 2. T2 weighted images in brain MRI of the patient with SSPE revealed hyperintense lesions bilaterally in the posterior areas but prominent on the right occipital lobe, mostly involving white matter.

te, allowing easy generalization of neuronal discharges, and the prolonged refractoriness was the cause of the slowly repetitive pattern. Fenyo and Hasznos claimed that the brainstem might play a role in the genesis of periodic discharges (13). The underlying mechanisms of the genesis of LPDs and GPDs are still not well known (1).

In our patient with SSPE, lesions in the MRI were seen prominently in the subcortical white matter, which actually does not imply that the cortical or subcortical grey matter is not involved. LPD activity on the right occipital region is consistent with the lesion topography, whereas, in the patient with MELAS, the lesions involved both cortex and subcortical white matter, but mainly the cortical area. There was an acute infarction in the right parietooccipital area over which we recorded LPDs. Although the lesion distribution seemed to differ between these two patients with respect to grey or white matter involvement, the result was long- interval GPDs and LPDs in both.

GPDs in MELAS have not been reported previously. There may be an association in part with the metabolic changes seen in MELAS, such as lactic acidosis, in the genesis of this EEG pattern.

It is known that GPDs in cases with SSPE become more prominent during sleep, and if routine EEG cannot show periodic discharges initially, the EEG should be recorded during sleep (1,4). We usually record EEGs with IV 10 mg diazepam injection (after recording routine EEG) if we suspect SSPE in our adult EEG laboratory. As reported before, GPDs are not suppressed with IV diazepam injection in SSPE cases; they even become more prominent, and the interval is shortened (14-18). We published our EEG study with the SSPE cases previously (5). Diazepam probably provokes sleep, and GPDs in SSPE are aggravated by diazepam-induced sleep. Contrary to this, discharges in the EEG of the case with MELAS were suppressed by IV diazepam injection, supporting the cortical involvement for the origin. Our patient did not have status epilepticus during the recording, but discharges, especially LPDs, might represent subclinical electrographic status epilepticus.

Coexistence of two topographically different periodic discharges in the same EEG simultaneously may occur in either cortical or subcortical weighted lesions, and different pathophysiological processes may cause the same electroencephalographic pattern. However, differences in response to the IV diazepam injections still support the different underlying mechanisms in the two conditions.

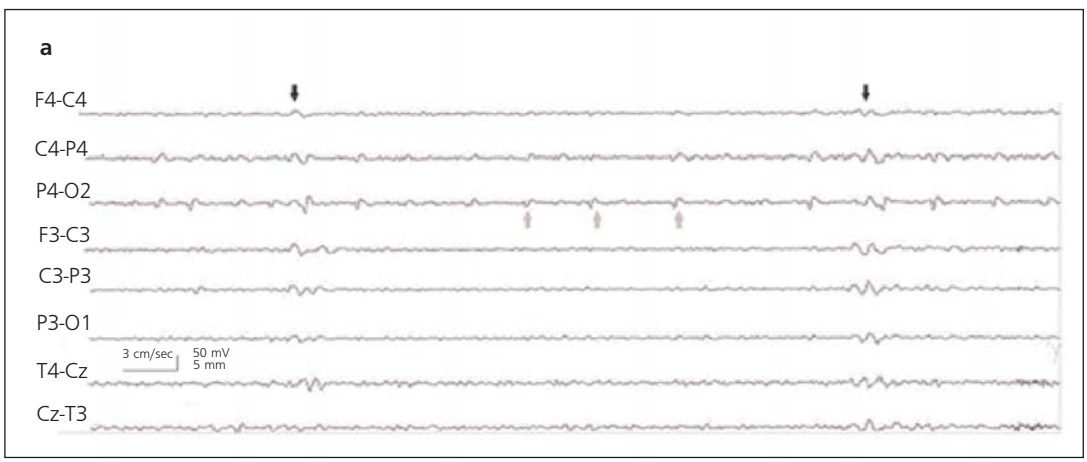

Figure 3a. EEG of the patient with MELAS syndrome: a) GPDs consisting of slow and slow sharp waves with 8-10-second intervals and right occipital LPDs in the EEG.

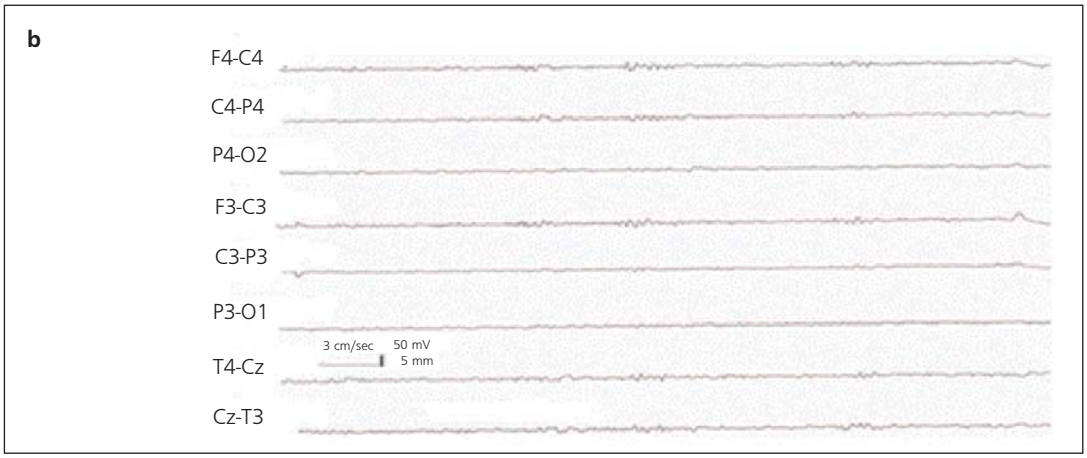

Figure 3b. b) GPDs and LPDs disappeared after IV 10 mg diazepam injection. Black and grey arrows indicate GPDs and LPDs, respectively. HF: 35 Hz; LF: 0.5 Hz (GPDs, generalized periodic discharges; LPDs, lateralized periodic discharges; MELAS, mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke-like episodes).

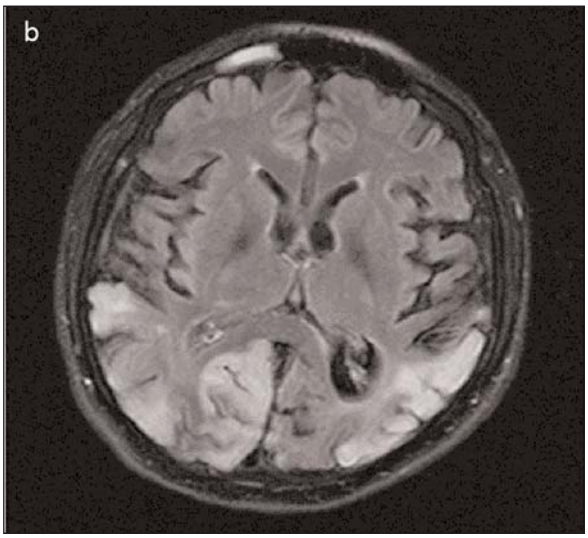

Figure 4. FLAIR images in the brain MRI of the patient with MELAS showed bilateral temporoparietooccipital lesions involving cortical area mostly.

REFERENCES

1. *Brenner RP, Schaul N. Periodic EEG patterns: classification, clinical correlation, and pathophysiology. J Clin Neurophysiol 1990;7:249-67.*
2. *Yemisci M, Gurer G, Saygi S, Ciger A. Generalised periodic epileptiform discharges: clinical features, neuroradiological evaluation and prognosis in 37 adult patients. Seizure 2003;12:465-72.*
3. *Hirsch LJ, Brenner RP, Drislane FW, So E, Kaplan PW, Jordan KG, et al. The ACNS subcommittee on research terminology for continuous EEG monitoring: proposed standardized terminology for rhythmic and periodic EEG patterns encountered in critically ill patients. J Clin Neurophysiol 2005;22:128-35.*
4. *Cobb W. The periodic events of subacute sclerosing leucoencephalitis. Electroencephalogr Clin Neurophysiol 1966;21:278-94.*
5. *Dogulu CF, Ciger A, Saygi S, Renda Y, Yalaz K. Atypical EEG findings in subacute sclerosing panencephalitis. Clin Electroencephalogr 1995;26:193-9.*
6. *Tulinius MH, Hagne I. EEG findings in children and adolescents with mitochondrial encephalomyopathies: a study of 25 cases. Brain Dev 1991;13:167-73.*
7. *Fujimoto S, Mizuno K, Shibata H, Kanayama M, Kobayashi M, Sugiyama N, et al. Serial electroencephalographic findings in patients with MELAS. Pediatr Neurol 1999;20:43-8.*
8. *Leff AP, McNabb AW, Hanna MG, Clarke CR, Larner AJ. Complex partial status epilepticus in late-onset MELAS. Epilepsia 1998;39:438-41.*
9. *Veggiotti P, Colamaria V, Dalla Bernardina B, Martelli A, Mangione D, Lanzi G. Epilepsia partialis continua in a case of MELAS: clinical and neurophysiological study. Neurophysiol Clin 1995;25:158-66.*
10. *Araki T, Suzuki J, Taniwaki Y, Ishido K, Kamikaseda K, Turuta Y, et al. A case of MELAS presenting complex partial status epilepticus. Rinsho Shinkeigaku 2001;41:487-90.*
11. *Corda D, Rosati G, Deiana GA, Sechi G. "Erratic" complex partial status epilepticus as a presenting feature of MELAS. Epilepsy Behav 2006;8:655-8.*
12. *Gloor P, Kalabay O, Giard N. The EEG in diffuse encephalopathies: electroencephalographic correlates of gray and white matter lesions. Brain 1968;91:779-802.*
13. *Fenyo E, Hasznos T. Periodic EEG complexes in subacute sclerosing panencephalitis: reactivity, response to drugs and respiratory relationships. Electroencephal Clin Neurophysiol 1964;16:446-50.*
14. *Bonifas-Galup P, Hamano K, Sebrosa CJ, Plouin P. Different clinical and electroencephalographic aspects of subacute sclerosing panencephalitis (SSPE). Apropos of 51 cases. Rev Electroencephalogr Neurophysiol Clin1983;13:224-31.*
15. *Anlar B, Yalaz K, Ustacelebi S. Symptoms and clinical signs, laboratory data in 80 cases of subacute sclerosing panencephalitis. Rev Neurol (Paris) 1988;144:829-32.*
16. *Malherbe V, Navelet Y, Tardieu M. Atypical electroencephalographic activity in terminal phase subacute sclerosing panencephalitis. Neurophysiol Clin 1991;21:183-8.*

17. *Sharp GB, Laney SM, Westmoreland BF, Groover RV. Atypical electroencephalographic pattern in a patient with subacute sclerosing panencephalitis. Electroencephalogr Clin Neurophysiol 1991;78:311-3.*

18. *Aydin OF, Senbil N, Gürer YK. Nonconvulsive status epilepticus on electroencephalography in a case with subacute sclerosing panencephalitis. J Child Neurol 2006;21:256-60.*

Yazışma Adresi/Address for Correspondence

Prof. Dr. Serap Saygı

Hacettepe Üniversitesi Tıp Fakültesi
Nöroloji Anabilim Dalı
Sıhhiye 06100 Ankara/Türkiye

E-posta: ssaygi@hacettepe.edu.tr

geliş tarihi/received 24/01/2011
kabul ediliş tarihi/accepted for publication 29/03/2011